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MALNUTRITION-INFLAMMATION SCORE PREDICTS SURVIVAL IN HEMODIALYSIS PATIENTS

Lada Trajceska[1], Gjulsen Selim[1], Stefan Arsov[2] Aleksandra Canevska[1]
[1]University Clinic of Nephrology, Skopje
[2]Institute of Epidemiology, Biostatistics and Medical Informatics, Skopje

Abstract

The short life span of dialysis patients is induced by traditional cardiovascular and non-traditional dialysis related factors such as inflammation, oxidative stress, protein energy malnutrition. Malnutrition-Inflammation Score (MIS) has been proposed as a new quantitative system for assessment of malnutrition and inflammation. In this study we sought to investigate the association of MIS and five-year-mortality in dialysis patients. In a prospective study were included 131 prevalent dialysis patients. Kalantar-Zadeh method (7) was used to calculate the malnutrition score. Patients were followed for five years. Kaplan-Meier survival and Cox-proportional mortality analysis were performed according to higher and lower malnutrition inflammation score, by cut-off value of 7. The mean age of study participants was 55.45 years and mean dialysis vintage was 111.04 months. After follow-up of 60 months 55 (42%) patients died from all-cause mortality and out of those 65% (36) were cardiovascular deaths. In comparative analysis among the survived and died patients, none of the inflammatory or nutritional variables such as CRP, albumin, creatinine, BMI or SGA significantly differed. There was a significantly longer survival among patients with lower MIS in respect of all-cause and cardiovascular mortality [49.28 ± 1.88 *vs.* 39.29± 3.53 months, p=0.011], [52.20 ± 1.7 *vs.* 45.07 ± 3.41, p=0.045], respectively. MIS emerged as a powerful predictor of all-cause and cardiovascular mortality through Cox regression analysis: HR 1.97 95%CI: (1.15 – 3.38), p=0.013; HR 1.063 95%CI-0.952-1.186, p=0.055), respectively. The malnutrition-inflammation score is a useful tool to predict outcomes. The key to improving survival and quality of life in dialysis patients could be gained by understanding of the malnutrition-inflammation complex syndrome and its interactions with cardiovascular disease and outcome.

Key words: dialysis, mortality, malnutrition inflammation complex, albumin, morbidity

Introduction

Mortality is very high in dialysis patients, with 55% dying within 5 years of initiating dialysis therapy [1-3]. The short life span of those patients is quite comparable with patients suffering from cancer [4,5]. The presence of cardiovascular disease is an important predictor of mortality in patients with end-stage renal disease as it accounts for almost 50% of deaths [6]. The high mortality rates are endured by traditional cardiovascular and non-traditional dialysis related factors such as inflammation, oxidative stress, protein energy malnutrition, together also known as malnutrition-inflammation complex syndrome. Malnutrition-Inflammation Score (MIS) has been proposed as a new quantitative system for assessment of malnutrition and inflammation [7], which are common important risk factors for increased morbidity and mortality in maintenance hemodialysis patients [8-10]. In this study we sought to investigate the association of MIS and five-year-mortality in dialysis patients.

Methods

In a prospective study were included 131 prevalent dialysis patients. Mid-week pre-dialysis blood samples were drawn for laboratory investigations. Clinical and nutritional data, cardiovascular and other comorbidities as chronic heart failure (CHF), coronary artery disease (CAD), chronic obstructive pulmonary disease, neurologic sequalae and malignances were extracted from medical charts. Patients were questioned for dietary intake and physically examined. Kalantar-Zadeh method (7) was used to calculate the malnutrition score. The MIS (7) incorporates seven components of the original Subjective Global Assessment (SGA) plus the body mass index (BMI), serum albumin and total iron-binding capacity (TIBC) or transferrin (Table 1). It has four sections (nutritional history, physical examination, BMI, and laboratory values) and 10 components. Each component has four levels of severity, from 0 (normal) to 3 (severely abnormal). The sum of all 10 MIS components can

range from 0 (normal) to 30 (severely malnourished); a higher score reflects a more severe degree of malnutrition and inflammation (Table 1). The five nutritional history-based components include: weight change, dietary intake, gastrointestinal symptoms, functional capacity, and comorbid conditions. In the current study, dialysis vintage was not included in the comorbidity components. The two physical examination components consist of the assessment of the subcutaneous body fat and signs of muscle wasting. In addition to the foregoing seven SGA-based components, the three MIS-unique sections include the BMI (>20, 18 to 19.99, 16 to 17.99, and <16 kg/m2), serum albumin (≥4.0, 3.5–3.9, 3.0–3.4 and <3.0 g/dl) and serum TIBC (≥250, 200–249, 150–200, and <150 mg/dl), the four increments of which are also scored from 0 through 3, respectively. Patients were followed up for 60 months for cardiovascular and all-cause mortality. Statistical methods: Continuous variables are shown as mean and SD, nominal as percentages. Kaplan Meier survival and Cox proportional mortality analysis were performed according to higher and lower malnutrition inflammation score, by cut-off value of 7.

MALNUTRITION INFLAMMATION SCORE (M.I.S)

(A) Patient's related medical history:				
1. Change in end dialysis dry weight (overall change in past 3-6 months):				
	0	1	2	3
1	No decrease in dry weight or weight loss < 9.5 kg	Minor weight loss (≥ 0.5 kg but < 1 kg)	Weight loss more than 1 kg but < 5%	weight loss > 5%
2. Dietary Intake:				
	0	1	2	3
2	Good appetite and no deterioration of the dietary intake pattern	Somewhat sub-optimal solid diet intake	Moderate overall decrease to full liquid diet	Hypo-caloric liquid to starvation
3. Gastrointestinal (GI) symptoms:				
	0	1	2	3
3	No symptoms with good appetite	Mild symptoms, poor appetite or nauseated occasionally	Occasional vomiting or moderate GI symptoms	Frequent diarrhea or vomiting or severe anorexia
4. Functional capacity (nutritionally related functional impairment)::				
	0	1	2	3
4	Normal to improved functional capacity, feeling fine	Occasional difficulty with baseline ambulation, or feeling tired frequently	Difficulty with otherwise independent activities (e.g. going to bathroom)	Bed/chair-ridden, or little to no physical activity
5. Co-morbidity, including number of years on dialysis:				
	0	1	2	3
5	On dialysis < 1 year and healthy otherwise	Dialyzed for 1-4 years, or mild co-morbidity (excluding MCC*)	Dialyzed > 4 years, or moderate co-morbidity (including one MCC*)	Any severe, multiple co-morbidity (2 or more MCC*)
(B) Physical Exam (according to SGA Criteria):				
6. Decreased fat stores or loss of subcutaneous fat (below eyes, triceps, biceps, chest):				
	0	1	2	3
6	Normal (no change)	Mild	Moderate	Severe
7. Signs of muscle wasting (temple, clavicle, scapula, ribs, quadriceps, knee, interosseous):				
	0	1	2	3
7	Normal (no change)	Mild	Moderate	Severe
(C) Body Mass Index:				
	0	1	2	3
8	BMI ≥ 20 kg/m²	BMI 18 - 19.99 kg/m²	BMI 16 - 17.99 kg/m²	BMI < 16 kg/m²
(D) Laboratory Parameters:				
9. Serum albumin				
	0	1	2	3
9	Albumin ≥ 4.0 g/dl	Albumin 3.5 - 3.9 g/dl	Albumin 3.0 - 3.4 g/dl	Albumin < 3.0 g/dl
10. Serum TIBC (Total Iron Binding Capacity) OR serum transferrin . Input value				
	0	1	2	3
10	TIBC ≥ 250 mg/dl Transferrin > 200 mg/dl	TIBC 200 -249 mg/dl Transferrin 170 -200 mg/dl	TIBC 150 -199 mg/dl Transferrin 150 -169 mg/dl	TIBC < 150 mg/dl Transferrin < 150 mg/dl

*MCC (Major Comorbid Conditions): include CHF class III or IV, full blown AIDS severe CAD, moderate to severe COPD, major neurologic sequelae, and metastatic malignancies or s/p recent chemotherapy.

Table 1. Calculation of MIS

Results

Patient characteristics are shown in Table 2. The mean age of study participants was 55.45 years and mean dialysis vintage was 111.04 months. Of all included patients, 57% were men and 18% had diabetes. Good dialysis adequacy was achieved in majority of patients, implying the mean Kt/V of 1.38. Patients were dialyzed from 3 to 5 hours per dialysis session. The laboratory nutritional indices such as albumin, hemoglobin and cholesterol were within expected ranges for dialysis population. Inflammation recognized by CRP varied more than other variables, in range from 0.4 to

57. Subjective global assessment and BMI values were used in the final nutritional inflammatory assessment, combined into the score MIS which ranged from 0-15.

The malnutrition-inflammation score distribution among patients is shown in Figure 1. The mean value was 5.7±2.8. The curve was bell shaped.

N=131	**Mean ± SD; No (%)**	**Range**
Men (%)	75 (57%)	
Diabetes (%)	24 (18%)	
Age (years)	55.45 ± 13.30	19 - 84
Vintage (months)	111.04 ± 72.95	5 - 349
Kt/V	1.38 ± 0.21	
Dialysis time (hours)	4.08 ± 0.22	3.63 – 5.0
PCR	1.02 ± 0.15	0.6 – 1.6
Hemoglobin (g/L)	116.36 ± 8.4	93 – 139
Albumin (g/L)	38.85 ± 2.5	30 – 45
CRP (ng/L)	7.06 ± 8.70	0.4 – 57
Total Cholesterol (mmol/L)	4.38 ± 1.01	2.5 – 8
TIBC (μmol/l)	225.85 ± 51.18	155.22 – 426.01
BMI (Kg/m^2)	23.74 ± 4.6	15.8 – 43.7
SGA	5.99 ± 0.94	3.4 – 7
MIS	5.75 ± 2.87	0 - 15

Table 2. Patients characteristics at the beginning of the study

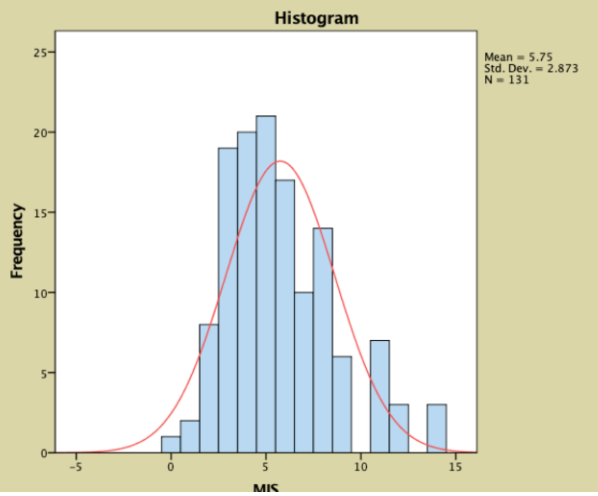

Figure 1. Bell shaped curve of MIS distribution among dialysis patients

After follow-up of 60 months, 55 (42%) patients died from all-cause mortality and out of those 65% (36) were cardiovascular deaths. The comparative analysis between the survived and died patients (Table 3) showed that none of the inflammatory or nutritional variables (CRP, albumin, creatinine, BMI or SGA) significantly differed.

Variable	Survived pts. N=76	Died pts N= 55	P (sig)
Age	51.72 ± 13.38	60.64 ± 19.71	0.000
Vintage	103.78 ± 74.11	121.14 ± 70.79	0.172
CRP	5.24 ± 6.17	5.84 ± 0.93	0.09
Albumin	39.01 ± 2.42	38.62 ± 2.70	0.397
Creatinine	976.37 ± 216.66	902.82 ± 192.56	0.440
BMI	23.89 ± 5.09	23.54 ± 3.90	0.650
SGA	6.11 ± 0.92	5.84 ± 0.93	0.107
MIS	5.41 ± 2.75	6.1 ± 3.01	0.200

Table 3. Comparison of survived and died patients

Figure 2 shows Kaplan Meier curves of survival for higher and lower MIS. A smaller number of patients died from all-cause and cardiovascular mortality in the group of patients with MIS below 7, compared to the group with MIS above 7: [32(36%) *vs.* 23(56%)], p<0.05; [21(23%) *vs.* 15(36%)], p<0.05, respectively. There was a significantly longer survival among patients with lower MIS in respect of all-cause and cardiovascular mortality [49.28 ± 1.88 *vs.* 39.29± 3.53 months, p=0.011], [52.20 ± 1.7 *vs.* 45.07 ± 3.41, p=0.045], respectively. MIS emerged as a powerful predictor of all-cause and cardiovascular mortality through Cox regression analysis: HR 1.97 95%CI:(1.15 – 3.38), p=0.013; HR 1.063 95%CI-0.952-1.186, p=0.055), respectively.

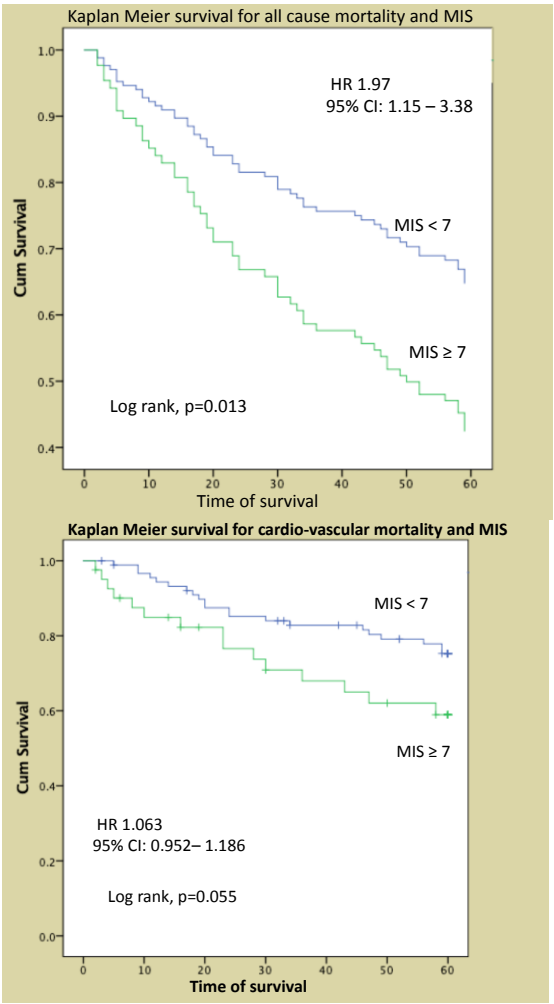

Figure 2. Kaplan Meier curves of survival, cardiovascular and all-cause mortality regarding MIS values

Discussion

Many recent studies have confirmed the malnutrition-inflammation score to be independent predictor of mortality in dialysis patients [9-11]. The PROHEMO study results indicated that MIS components associated with mortality were not the same associated with all patients' outcomes. Weight change, comorbidity, muscle wasting, and albumin were the MIS components indicating associations between poor nutrition and higher mortality. By contrast, gastrointestinal symptoms and functional capacity were the MIS components denoting detrimental associations of poorer nutritional status with outcomes [12]. Another study found the SGA and MIS to be both independent predictors of mortality [13]. In Pisetkul's study the MIS was superior to the conventional SGA as a predictor of short-term outcome in MHD patients [10]. In our comparative analysis on nutritional and inflammatory data between the survived and died patients, there was no significant difference for SGA, albumin, creatinine, CRP, similar to Rambods' study [9]. But, when those factors interpolated in the component score, MIS emerged as a powerful predictor of both all-cause and cardiovascular mortality in Kaplan Meier and Cox-regression analysis. The need of merging both the malnutrition and inflammation into a unique score was also confirmed in the latest Epifanio's study in 2018, which found that the subjective scoring systems was more sensitive to malnutrition, and altogether anthropometric indicators may result in an early detection of mortality risk in this population. On the other hand, inflammation in dialysis, as assessed by C-reactive protein, was not only related to cardiometabolic alterations, but was also one of the key-points in the development of malnutrition, exacerbated by the state of oxidative stress [14]. The value of MIS ranges from 0-30 [7]. In the recent studies, the cut-off value of MIS that determined higher mortality rates, was above 7 [10,11]. In our study, the patients' mortality was analyzed according to MIS level above and below 7 and the difference was also found significant for the all-cause and cardiovascular mortality.

Conclusions:

The strongest and most common correlates of death in dialysis patients are not conventional cardiovascular risk factors, but markers of protein-energy malnutrition and inflammation, together also known as malnutrition-inflammation complex syndrome. The malnutrition-inflammation score is a useful tool to predict outcomes. The key to improving survival and quality of life in dialysis patients could be gained by understanding of the malnutrition-inflammation complex syndrome and its interactions with cardiovascular disease and outcome.

References

1. Moist LM, Fenton S, Kim JS, et al. Canadian Organ Replacement Register (CORR): reflecting the past and embracing the future. Annual report: Treatment of End-Stage Organ Failure in Canada, 2003 to 2012.Can J Kidney Health Dis. 2014; 1:26.
2. Covic, A., Gusbeth-Tatomir, P., and Goldsmith, D. Negative outcome studies in end-stage renal disease: how dark are the storm clouds?. Nephrol Dial Transplant. 2008; 23: 56–61.
3. Saran R, Li Y, Robinson B, et al. US Renal Data System 2015 Annual Data Report: epidemiology of kidney disease in the United States. *Am J Kidney Dis*. 2016; 67(3) (suppl 1):S1-S434.
4. Autier, P., Boniol, M., LaVecchia, C. et al. Disparities in breast cancer mortality trends between 30 European countries: retrospective trend analysis of WHO mortality database. BMJ. 2010; 341: 448.
5. Mokdad, A.H., Dwyer-Lindgren, L., Fitzmaurice, C. et al. Trends and patterns of disparities in cancer mortality among US counties, 1980-2014. JAMA. 2017; 31(7): 388–406.
6. Rattanasompattikul M, Chanchairujira K, On-Ajyooth L, Chanchairujira T. Evaluation of atherosclerosis, arterial stiffness and related risk factors in chronic hemodialysis patients in Siriraj Hospital. J Med Assoc Thai. 2011; 94 Suppl 1:S117-24.
7. Kalantar-Zadeh K, Kopple JD, Block G, Humphreys MH. A malnutrition-inflammation score is correlated with morbidity and mortality in maintenance hemodialysis patients. Am J Kidney Dis. 2001; 38(6):1251–1263.

8. Landray MJ, Thambyrajah J, McGlynn FJ, et al. Epidemiological evaluation of known and suspected cardiovascular risk factors in chronic renal impairment. Am J Kidney Dis 2001; 38:537.
9. Rambod M, Bross R, Zitterkoph J, et al. Association of Malnutrition-Inflammation Score with quality of life and mortality in hemodialysis patients: a 5-year prospective cohort study. *Am J Kidney Dis*. 2008; 53(2):298-309.
10. Pisetkul C1, Chanchairujira K, Chotipanvittayakul N, Ong-Ajyooth L, Chanchairujira T. Malnutrition-inflammation score associated with atherosclerosis, inflammation and short-term outcome in hemodialysis patients. J Med Assoc Thai. 2010; 93 Suppl 1:S147-56.
11. Borges M, Clementoni C et al. Malnutrition Inflammation Score cut-off predicting mortality in maintenance hemodialysis patients. Clin. Nutr. ESPEN 2017; 17:63-7.
12. Lopes MB, Silva LF, Lopes GB et al. Additional Contribution of the Malnutrition-Inflammation Score to Predict Mortality and Patient-Reported Outcomes as Compared With Its Components in a Cohort of African Descent Hemodialysis Patients. J Ren Nutr.2017; 27(1):45-52.
13. Perez V. Are Nutritional Composed Scoring Systems and Protein-Energy Wasting Score Associated With Mortality in Maintenance Hemodialysis Patients?J Ren Nutr. 2016; 26(3):183-9.
14. Epifanio APS, Balbino KP, Ribeiro KP et al. Clinical-nutritional, inflammatory and oxidative stress predictors in hemodialysis mortality: a review. Nutr Hosp.2018; 35(2):461-8.